A 90 Day Subchronic Toxicity Subcutaneous Implant Study in Rats Administered Room Temperature Vulcanized (RTV) Shell, Diaphragm Valve and Plug Assembly, Leaf Valve and Overlay Assembly, and Patch and Overlay Assembly

SUMMARY AND CONCLUSION

The subcutaneous implantation of the test articles, RTV Shell, Diaphragm Valve/Plug, Leaf Valve/Overlay or Patch/Overlay, resulted in an immediate inflammatory reaction at the site of implantation. Grossly the reaction consisted primarily of edema. Occasionally, eschar was noted during the first two weeks in the test article implanted groups. Edema was noted in the Sham Control group the first day after surgery.

Microscopically the implant site lesions were characterized by multiloculated, cyst-like areas containing fragments of transparent material (test article) surrounded by individual thin fibrous capsules. In some cases, the entire area was surrounded by a thin fibrous capsule. The tissue reaction consisted of macrophage aggregates, multinucleated foreign body giant cells, pigment-laden macrophages, and/or mononuclear cell infiltrates. The reaction observed among the four implanted groups was similar in type and severity. Changes noted in the Sham Control group was limited to focal dermal fibrosis at the incision sites.

Histopathological evaluation of other tissues after 90 days of exposure to the test articles revealed a low incidence of a variety of lesions. With the exception of implant site lesions, the lesions observed were considered to be typical for Fischer 344 rats of this age.

No evidence of systemic toxicity attributable to the implantation of the test articles was observed in any of the other parameters that were evaluated, including body weight, hematology and serum chemistry, organ weights (absolute and relative to brain and body weight) and gross pathology.